

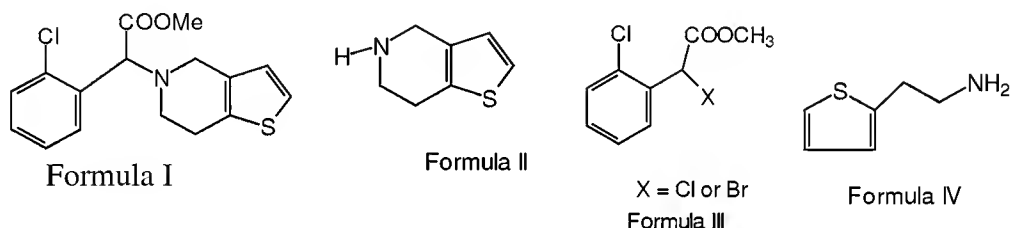
Amendments to the Claims:

Amendments to the Claims :

The following listing of claims replaces all prior versions and listings of claims in this application:

1-31. (cancelled)

32. (withdrawn) A process for making clopidogrel of Formula I starting from 2-(2-thienyl)ethylamine characterized in that the said process comprising



i) reacting 2-(2-thienyl)ethylamine of Formula IV with paraformaldehyde to form 4,5,6,7-tetrahydrothieno(3,2-c)pyridine of Formula II, wherein the step takes place in a single vessel without isolation of 2-(2-thienyl)ethyl formimine; and

ii) reacting the compound of Formula II with a halobenzene derivative of Formula III, wherein X= Cl or Br, in presence of a base in a solvent selected from dichloroethane or water or a mixture of water and hydrocarbon/chlorinated hydrocarbon solvents to obtain clopidogrel and isolating said clopidogrel as free base or its salt.

33. (withdrawn) The process of claim 32, wherein the step i) is performed in a solvent selected from aliphatic, aromatic hydrocarbons and chlorinated hydrocarbons.

34. (withdrawn) The process of claim 33, wherein the solvent is dichloroethane.
35. (withdrawn) The process of claim 32, wherein 2-(2-thienyl)ethyl formimine is formed in-situ by effective removal of water at reflux temperature and cyclized in presence of anhydrous hydrochloric acid.
36. (withdrawn) The process of claim 32, wherein said 4,5,6,7-tetrahydrothieno(3,2-c)pyridine is formed at a temperature ranging from about 60°C to 90°C.
37. (withdrawn) The process of claim 32, wherein step ii) is carried out in dichloroethane.
38. (withdrawn) The process of claim 32, wherein the base is selected from trialkyl amines.
39. (withdrawn) The process of claim 38, wherein the base is triethyl amine.
40. (withdrawn) The process of in claim 32, wherein step ii) takes place at a temperature of 50°C to 80°C.
41. (withdrawn) The process of claim 32, wherein the clopidogrel is prepared in a single-pot procedure without isolation of intermediates 4,5,6,7-tetrahydrothieno(3,2-c)pyridine or its salts.

42. (withdrawn) The process of claim 32, wherein step i) takes place in the presence of an acid catalyst.

43. (withdrawn) The process of claim 42, wherein the acid catalyst is HCl.

44. (withdrawn) A process for preparation of clopidogrel of Formula I comprising the step of reacting 4,5,6,7-tetrahydrothieno(3,2-C)pyridine of formula II or its salt with a halobenzene derivative of Formula III in presence of a base in a solvent, wherein the solvent is chlorinated hydrocarbon, water or a mixture of water and hydrocarbon solvents selected from aliphatic, aromatic and chlorinated hydrocarbons.

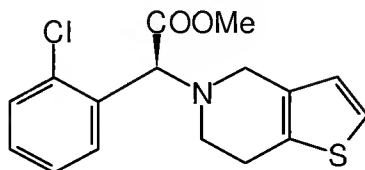
45. (withdrawn) The process of claim 44, wherein the solvent is a combination of dichloroethane and water.

46. (withdrawn) The process of claim 44, wherein the base is sodium carbonate or potassium carbonate.

47. (withdrawn) The process of claim 44, wherein reaction is performed at a temperature of 20°C to 40°C.

48. (withdrawn) The process of claim 44, wherein the compound of Formula III is methyl-1-bromo-(2-chlorophenyl)acetate.

49. (withdrawn) The process of claim 44, further comprising the steps of treating said clopidogrel of Formula I with levo-rotatory camphor sulphonic acid in a solvent system of polar and apolar/weakly polar solvents; and obtaining substantially pure dextrorotatory clopidogrel of Formula IA.



Formula IA

50. (withdrawn) The process of claim 49, wherein the solvent system is acetone and dichloromethane; acetone and toluene; or acetone and cyclohexane

51. (withdrawn) The process of claim 50, wherein the combination solvent is acetone **and** dichloromethane.

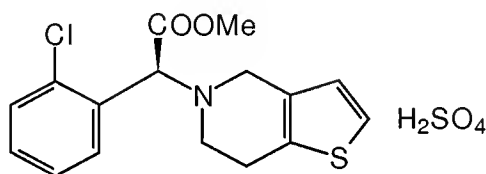
52. (withdrawn) The process of claim 51, wherein the ratio of acetone and dichloromethane is 10:1.0.

53. (withdrawn) A process for preparation of dextrorotatory clopidogrel or its salt comprising the step of resolving racemic clopidogrel with levo-rotatory camphor sulphonic acid in a solvent system of polar and apolar/weakly polar solvents to obtain substantially pure dextrorotatory clopidogrel of Formula IA.

54. (withdrawn) The process of claim 53, wherein the solvent system is acetone:dichloromethane, acetone: toluene, or acetone: cyclohexane.

55. (withdrawn) The process of claim 54, wherein the combination solvent is acetone:dichloromethane.

56. (currently amended) An process for making Form I crystals of (+)-(S)-clopidogrel hydrogen sulphate of Formula IB comprising the steps of:



Formula IB

- i) dissolving methyl (+)-(S)- α -(2-chlorophenyl)-4,5,6,7-tetrahydrothieno[3,2-C]pyridine-5-acetate ((+)-(S)-clopidogrel base) in a solvent selected from methyl propyl ketone, methyl isopropyl ketone, diethyl ketone, mixture of ketone solvents, ethyl acetate - methyl propyl ketone mixture, ethyl acetate-methyl isopropyl ketone mixture, and ethyl acetate-diethyl ketone mixture;
- ii) cooling said clopidogrel base solution;
- iii) adding ~~concentrated~~ sulphuric acid to said cooled solution to form a salt mixture;
- iv) maintaining said salt mixture to precipitate (+)-(S)-clopidogrel hydrogen sulphate in Form I; and

v) recovering said crystals of Form I.

57. (previously presented) The process of claims 56, wherein said mixture of ketone solvents are mixtures of methyl propyl ketone and methyl isopropyl ketone, mixture of methyl propyl ketone and diethyl ketone, or mixture of methyl isopropyl ketone and diethyl ketone.

58. (previously presented) The process of claim 56, wherein step ii) involves cooling to a temperature range of -10 to 20 °C.

59. (previously presented) The process of claim 56, wherein step iii) is carried out while maintaining reaction solution temperature at -10 to 10° C.

60. (previously presented) The process of claim 56, wherein the solution is seeded with Form I prior to addition of sulphuric acid.

61. (previously presented) The process of claim 56, wherein the mixture of step iv) is maintained at a temperature range of 10 ° to 30 ° C.

62. (previously presented) The process of claim 61, wherein the mixture of step iv) is maintained at 10 ° to 30 ° C for 8 to 15 hours.

63. (previously presented) The process of claim 56, wherein the solvent is methylpropyl ketone.

64. (previously presented) The process of claim 56, wherein the solvent is methylisopropyl ketone.

65. (previously presented) The process of claim 56, wherein the solvent is ethyl acetate-methylpropyl ketone.

66. (previously presented) The process of claim 56, wherein the solvent is ethyl acetate-methylisopropyl ketone.

67. (previously presented) The process of claim 56, wherein the solvent is methyl propyl ketone and methyl isopropyl ketone.

68. (withdrawn) A process for making Form I crystals of (+)-(S)-clopidogrel hydrogen sulphate of Formula IB, said process comprising:

i) dissolving methyl (+)-(S)- α -(2-chlorophenyl)-4,5,6,7-tetrahydrothieno[3,2-C]pyridine-5-acetate ((+)-(S)-clopidogrel base) in ethyl acetate;

ii) cooling to a temperature of 18° to 20° C;

iii) mixing said cooled solution with concentrated sulphuric acid in which the temperature not exceeding 30°C;

iv) maintaining the salt mixture at 28° to 30° C for 7 to 10 hours to effect precipitation of (+)-(S)-clopidogrel hydrogen sulphate in Form I; and

v) recovering said crystals of Form I.

69. (withdrawn) The process of claim 68, wherein step iii) is carried out while maintaining the temperature at 18 to 24° C.

70. (withdrawn) The process of claim 68, wherein the strength of said sulphuric acid is about 95 to 98 %.

71. (withdrawn) The process of claim 68, wherein the molar ratio of sulphuric acid used is 1.02 to 1.1 relative to (+)-(S)-clopidogrel base.

72. (withdrawn) A clopidogrel Form I prepared according to claim 1 and having the Powder X-ray diffraction pattern as substantially given in Figure 1.

73. (withdrawn) A pharmaceutical composition characterized in that the clopidogrel prepared according to claim 1 and having the Powder X-ray diffraction pattern as substantially given in Figure 1 is put into a pharmaceutically acceptable dosage form.

74. (new) A process for preparation of Form I of (+)-(S)-clopidogrel hydrogen sulphate comprising isolation of (+)-(S)-clopidogrel hydrogen sulphate in crystalline Form I from a solvent selected from methylpropylketone, methyl isopropylketone, diethyl ketone, mixture of ketone solvents, and mixture of ketone solvent with organic solvent.

75. (new) The process as claimed in claim 74, wherein the organic solvent is ethyl acetate.